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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,897	06/07/2005	Ana Isabel Sanz Molinero	BJS-4982-5	8027

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,897	SANZ MOLINERO, ANA ISABEL	
	Examiner	Art Unit	
	STUART F. BAUM	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/6/20120*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,10,12-17,19-23,29,44-47,49-51 and 53-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,10,12-17,19-23,29,44,45,47,49-51 and 53-56* is/are rejected.

7)☒ Claim(s) *46* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/2/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 4/6/2010 has been entered.

2. Claims 1-4, 10, 12-17, 19-23, 29, 44-47, 49-51 and 53-56 are pending.

Claims 5-9, 11, 18, 24-28, 30-43 and 52 have been canceled.

3. Claims 1-4, 10, 12-17, 19-23, 29, 44-47, 49-51 and 53-56, including SEQ ID NO:1, 2, 5, 51, 7, 8 and 9 are examined in the present office action.

4. Rejections and objections not set forth below are withdrawn.

5. The text of those sections of Title 35, U.S. Code not included in this office action can be found in a prior office action.

Written Description

6. Claims 1-4, 10, 12-17, 19-23, 29, 44-45, 47, 49-51 and 53-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to methods comprising transforming a plant with a sequence encoding a 2xC2H2 zinc finger protein, said 2xC2H2 zinc finger protein comprising motifs (i) - (iv): wherein (i) comprises SEQ ID NO:5 or 51, motif (ii) comprises SEQ ID NO:7, motif (iii) comprises SEQ ID NO:8 and motif (iv) comprises SEQ ID NO:9, or wherein said 2xC2H2 protein is encoded by a nucleic acid capable of completely hybridizing with SEQ ID NO:1, or wherein said 2xC2H2 protein comprises a sequences having 80% homology to SEQ ID NO:2.

Applicant discloses SEQ ID NO's:1, 2, 5, 51, 7, 8, and 9.

The Applicant does not identify essential amino acids of any of the amino acid motifs of SEQ ID NO:5, 51, 7, 8 and 9 nor does Applicant describe any polynucleotide sequences that hybridizes to SEQ ID NO:1 under any conditions or that encode a 2xC2H2 zinc finger protein having 80% homology to SEQ ID NO:2 that has the same activity as the protein encoded by SEQ ID NO:1.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants also fail to describe a representative number of polynucleotide sequences that comprise the recited motifs or that hybridize under any condition to SEQ ID NO:1 and encode a 2xC2H2 protein that when over-expressed produces the desired result. Applicants only disclose SEQ ID NO's:5, 7-9 and SEQ ID NO:1 encoding SEQ ID NO:2. Furthermore, Applicants fail to

describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the claimed proteins, it remains unclear what features identify said proteins. Since the genus of said proteins and the genus of polynucleotides that hybridize under any condition to SEQ ID NO:1 that encodes a plant 2xC2H2 zinc finger protein operable in applicant's invention has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Applicant's arguments filed 4/6/2010 have been fully considered but they are not persuasive.

Applicants contend methods to identify orthologous and paralogous sequences are taught in the specification pages 14-15 and a list of homologous sequences are provided on pages 15 and 16 (page 9 of Remarks, 4th paragraph).

The Office contends Applicants have not disclosed any alternative splice variants , allelic variants, homologues, derivatives or active fragments or a sequence that exhibits 80% sequence identity to SEQ ID NO:2 that are operable in Applicants' invention. The Office contends the list of sequences on page 15 have not been shown to produce the same effect as SEQ ID NO:1. For example, Accession Number BAA21923 is a zinc finger protein but does not comprise SEQ ID NO:9 and it is only 166 amino acids, whereas Applicants' SEQ ID NO:2 is 225 amino acids. The Office contends Applicants have presented sequences that are in the 2XC2H2 gene family but they have not disclosed all the essential regions of a protein that are required to produce the desired result and Applicants have not disclosed a representative number of sequences from a

representative number of plant species that encode a polypeptide falling within the scope of the claimed invention that when transformed into a plant produces the desired result.

Scope of Enablement

7. Claims 1-4, 10, 12-17, 19-23, 29, 44-45, 47, 49-51 and 53-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for increasing plant yield, method for increasing leaf surface area, method for prolonging vegetative growth phase and method for the production of a transgenic plant having increased yield comprising transforming a plant with a construct comprising a constitutive promoter operably linked to SEQ ID NO:1 encoding SEQ ID NO:2, does not reasonably provide enablement for said methods comprising transforming a plant with a nucleic acid sequence encoding a 2xC2H2 zinc finger protein comprising motifs (i)-(iv), as recited in claim 1, or wherein the protein is encoded by a sequence that hybridizes to SEQ ID NO:1 under any conditions or wherein the zinc finger protein has 80% homology to SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands,* 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior

art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to methods comprising transforming a plant with a sequence encoding a 2xC2H2 zinc finger protein, said 2xC2H2 zinc finger protein comprising motifs (i) - (iv): wherein (i) comprises SEQ ID NO:5 or 51, motif (ii) comprises SEQ ID NO:7, motif (iii) comprises SEQ ID NO:8 and motif (iv) comprises SEQ ID NO:9, or wherein said 2xC2H2 protein is encoded by a nucleic acid capable of completely hybridizing with SEQ ID NO:1, or wherein said 2xC2H2 protein has 80% homology tto SEQ ID NO:2.

Applicants state "A gene encoding an STZ protein was amplified by PCR from Arabidopsis thaliana seedling cDNA library" (page 35, lines 32-33), but Applicants do not disclose the primers or reaction conditions used to isolate said nucleic acid. Applicants disclose said nucleic acid was operably linked to the rice GOS2 constitutive promoter and transformed into rice (page 36, lines 14-23). Applicants disclose the resultant T1 or T2 generations containing at least one copy of the nucleic acid exhibited increased biomass (page 38, line 19), increased above ground area of the plant (page 38, line 22), more filled seeds (page 40, lines 5-7), increased seed weight (page 40, lines 20-22), increased number of seeds per plant (page 42, lines 14-end of the page), increased root growth (page 44, lines 1-19) and increased leaf width (page 44, lines 21-34).

Applicant's claims are broadly drawn to any 2xC2H2 protein having motifs (i)-(iv), wherein motifs (i)-(iv) are SEQ ID NO:5, 7, 8 and 9, respectively. The Office contends Applicant has not adequately disclosed in the specification and recited in the claims all of the amino acids that are conserved and required for a protein with the correct activity to be operable

in Applicant's invention. In short, Applicant's claims are drawn to a genus of proteins that would produce unpredictable results when used in Applicant's invention. The state-of-the-art teaches not all 2xC2H2 type of zinc finger proteins have the same function in plants. Takatsuji et al (1994, The Plant Cell (6):947-958) teach the EPF1 zinc finger protein has two canonical C2H2 zinc finger motifs that is expressed specifically in petals and interacts with the promoter region of the 5-enolpyruvyishikimate-3-phosphate synthase gene in petunia (page 947, right column and abstract) (See sequence search result of SEQ ID NO:2 in which the four domains are highlighted by a line over the domain). Ciftci-Yilmaz et al (2008, Cell. Mol. Life Sci. (65):1150-1160) teach the subclass of zinc finger proteins that has two C2H2 zinc finger contains 18 members, of which Applicant's SEQ ID NO:2 is a member (Zat10 is identical to Applicant's SEQ ID NO:2) and comprise SEQ ID NO:5 (a QALGGH domain) and an EAR domain (SEQ ID NO:7) and a B-box (nuclear localization sequence) and are repressors that are involved in plant defense and stress response (page 1154). The Office contends Applicant and the prior art are silent as to which 2xC2H2 protein comprising the four motifs will give the expected result.

In addition, Applicant has not disclosed how one makes or isolates any of the sequences that are encompassed by Applicant's broad claims. Applicant has not taught which regions of the respective polynucleotides can be used to amplify any of said polynucleotides or which regions can be used as a probe to isolate any of said polynucleotide sequences. The instant specification fails to provide guidance for which amino acids, other then those encompassed in SEQ ID NO:5, 7, 8 and 9, of the protein encoded by SEQ ID NO:1 can be altered, the type of alteration, and which amino acids must not be changed, to maintain activity of the encoded

protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional protein.

The Office contends Applicant has not disclosed all the essential amino acids of the encoded 2xC2H2 protein. This is evidenced by an alignment between SEQ ID NO:2 and 27 of the instant application. Comparing the two sequences reveals conserved amino acids other than those in the claimed motifs. Therefore, the claimed encoded 2xC2H2 protein comprising motifs (i)-(iv) lacks essential amino acids required by the protein to be active. (see attached protein alignment in Applicant's remarks filed 5/22/2009).

The state-of-the-art teaches specific amino acids within the zinc finger are responsible for specific DNA binding. Takatsuji (1996, Biochemical and Biophysical Research Communication 224:219-223) teach that a single amino acid in the second zinc finger is responsible for the difference in target sequence binding. Therefore, the Office contends that Applicant has not disclosed all the essential amino acids that are required for the proper activity of the claimed polypeptide.

Applicants claims are drawn to nucleic acid sequences that hybridize to SEQ ID NO:1 under any conditions, but the state-of-the-art teaches isolating DNA fragments using even stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65^0C (page 859, left column, 2^{nd} paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of

sequence differences comprising a 99bp insertion and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2).

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of SEQ ID NO:1 as probes or by designing primers to undisclosed regions of SEQ ID NO:2 and isolating or amplifying fragments, subcloning the fragments, producing expression vectors and transforming plants therewith, in order to identify those, if any, that when over-expressed produce a plant exhibiting increased yield, increased leaf surface area and increased vegetative state, when compared to a non-transformed plant.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Applicant's arguments filed 4/6/2010 have been fully considered but they are not persuasive.

Applicant states “moreover, as noted above, the sequences of the claims are highly conserved in zinc finger proteins throughout species and therefore would be necessary for function" (page 9 of Remarks, 2nd full paragraph). Applicant urges the Examiner to appreciate that the claims define the use of the recited sequences to achieve certain yield-enhancing traits in plants.

Claim 1 as currently amended is directed toward a polypeptide comprising four motifs, i.e., a sequence having SEQ ID NO:5, 7, 8 and 9. The recitation of a polypeptide comprising four motifs represents a partial structure. That is, the claimed polypeptides share SEQ ID NO:5, 7, 8 and 9 but no structure/function correlation has been presented. Applicant has not disclosed how one skilled in the art would determine which polypeptides having SEQ ID NO:5, 7, 8 and 9 also have the requisite structure to be operable in Applicant's invention. Applicant is claiming a genus of polypeptides based on four motifs comprising about 30 amino acids. Applicant is silent about the rest of the amino acids that are required for the claimed polypeptide. There is no teaching in the specification regarding which amino acids can be varied while retaining the required activity to produce a plant having increased yield, increased leaf area or prolonged vegetative growth. Consequently, there is no information about which amino acids can vary from SEQ ID NO:2 in the claimed genus of polypeptides and still retain the catalytic activity.

Briefly, for claims drawn to 80% identity to SEQ ID NO:2, Applicant has not taught which of the claimed sequences have the proper activity that when increased produce the desired result. Applicant has only disclosed the structure of SEQ ID NO:2.

Therefore, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement *(In re Fisher,* 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988).

8. Claims drawn to method for increasing plant yield, method for increasing leaf surface area or method for prolonging vegetative growth are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest a method for increasing plant yield, leaf surface area or prolonging vegetative growth comprising transforming a plant with a nucleic acid molecule encoding SEQ ID NO:2 and growing the plant under conditions promoting plant growth and selecting a plant having increased plant yield, leaf surface area or prolonged vegetative growth, respectively.

9. Claim 46 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

10. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached at 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Stuart F. Baum/
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Art Unit 1638
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